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AUTHORS ALONE ARE RESPONSIBLE FOR OPINIONS EXPRESSED IN THEIR CONTRIBUTIONS

MAHLON ASHFORD, *Editor*

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BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

MARCH 1945

SCIENTIFIC HUMANISM IN THIS CHANGING WORLD*

Presidential Address

W. W. Herrick

You have seen fit to confer upon me an outstanding honor, the Presidency of The New York Academy of Medicine. To one who has devoted his years to the teaching and practice of his calling and to the perhaps too sedulous avoidance of executive duties and of office, your mandate brings with it a lively awareness of limitations, limitations of experience and, I fear, of capacity.

That this mantle, which has descended upon my shoulders from those of the medically distinguished of the past, be worn with no diminution of lustre, I bespeak your kindly tolerance and your generous coöperation.

I am bound to say, however, that I assume it and the attendant obligations in no shrinking spirit; but rather in that expressed by the phrase of Oliver Wendell Holmes: "I am too much in earnest for either humility or vanity."

It has been said that an institution is but the lengthened shadow of a man. This, our Academy, is the almost century-long shadow of a few

* Delivered at the Annual Meeting of The New York Academy of Medicine, January 4, 1945.

medical leaders who, in 1847, first brought forward plans for its organization. This period in the history of our country has been called the time of decision; perhaps it also was such in medicine. In that year Virchow founded his *Archiv* and Pasteur graduated from the Ecole Normale. A Boston dentist had just brought to surgery the gift of anesthesia with the result that operations previously deemed impossible were undertaken. Valentine Mott, one of our founders, ligated the innominate artery, an unheard of surgical feat. Contributions such as that of Dr. Holmes on the Contagiousness of Puerperal Fever had given a new and stimulating aspect to medical problems. The negative contribution of Hahnemann made itself felt, as the public, ever ready to take the easier path, found the dilutions of Homeopathy certainly more agreeable and at times as efficacious as calomel and the lancet. The regular practitioners of the day felt the need to band together for mutual support and for the elevation of the standards of medical practice. Aware also of the ferment and progress about them, they declared it their further purpose to improve medical education and to contribute to medical literature. Shortly thereafter another primary purpose was added, the promotion of public health. As time has passed, the emphasis has gradually shifted to education, public health, and the dissemination of information on medical matters to the public.

Review of Academy programs uncovers a history of medicine since 1847. Papers describing the advances in surgical technique, the result of the use of anesthetics, occupy much of the earlier volumes. Studies in pathology, case reports, and matters of public health also may be found. With the work of Virchow the era of cellular pathology and of medicine based thereon is spread from the rostrum of this Academy. Here Charles L. Loomis and Edward Janeway, former Presidents, also Delafield and Prudden, among others of our fellowship, were pioneers in bringing pathologic anatomy into direct relation to bedside medicine. Austin Flint, an early President, brought physical diagnosis to its most finished stage. The next era, springing from the work of Pasteur, Koch, and Lister, was that of bacteriology. A president of this Academy protested against the seemingly too ready and widespread acceptance of bacteria in the causation of disease, and doubted if Pasteur had found a permanent place in medical science because of his polemical tendencies; nevertheless, progress in this phase of medicine continued, and the Academy played its part in making it public.

Later milestones in the widening scope of our profession may be considered the application of laboratory methods of chemistry and physics which have made clinical medicine much more precise and, last of all, the renewal of our faith in therapeutics crowned by the magical effects of the sulfonamides and of penicillin. There is no phase of these major steps in medical progress in which the Academy has not had its share and few indeed to which the Academy fellowship has not contributed.

Now we face a new era. The greatest war of all time must ere long come to a close bringing to our country and to our profession and to this Academy new obligations and new fields of labor. American medicine serves in every part of the world and everywhere it has met the challenge of great and compelling opportunity. It shall play its part in the reorganization of the world and may well be a great factor in the promotion of peace. To this end we must be assured that our own house is in order and our own capacity to serve remains unhampered.

In two years, the Academy will celebrate its centennial. It is not too early to begin to prepare for an occasion which should be notable in the medical progress not only of this city, but of the country. There are few medical organizations of equal importance that are more ancient. The Academy of Philadelphia is considerably older, having been founded in 1777. The American Medical Association is but one year our senior. At the 50th anniversary of the Academy, the then president of the United States made an address. In this, Grover Cleveland chided the medical profession because, in contrast to his boyhood days, the doctor of 1897 so seldom appeared in public life and so rarely held office. If, at that time, public office and medical practice were incompatible, how much more so today when one considers the additions to knowledge which must be compassed by the physician. Not so much from choice as from necessity is it that the doctor avoids office. By training and tradition the problems of the individual absorb and concern him rather than the larger matters of public life. The doctor has not looked at politics. Politics, however, is beginning to look at the doctor. It is beginning to see in the field of medicine a new instrument of power with rich possibilities of a domination which may well affect seriously many long established practices of proven value. If the physician is to maintain that freedom of action which has given to our country an unequalled medical service, it may be necessary for him to

follow the advice of Grover Cleveland and take a more active part in public affairs.

Already the Academy has taken cognizance of this situation in the work of the Committee on Medicine and the Changing Order. Physicians, publicists, social workers, laymen and holders of public office have met weekly for the discussion of every phase of this problem. The report of this committee will represent the most detailed and authoritative study of this complicated subject: it should be highly influential in securing appropriate legislation affecting the future practice of medicine in the United States.

Medicine has no small part to play in this changing order; it has the primary obligation of safeguarding the public health. This it can do best by the maintenance of its present high standards and by judicious action in any movement that threatens to lower those standards. Without abandoning its traditional practice of remaining aloof from politics, the Academy has the duty of bringing to bear the wise and expert counsel it commands. Certain social and political trends of the times have important biological implications. The experience of the profession in the practical aspects of sociology and of psychology, its intimate contact with the reactions of mankind to environmental changes of all sorts, gives weight to our opinions and judgments. It is proper that some of these be considered in no partisan spirit, but in a humble search for the truth.

There is a certain pessimistic philosophy abroad, not popular at any time, least of all in an election year; one in many of its aspects quite fallacious, yet with just enough validity to be arresting and with some relation to our problem. This philosophy* holds that the mass man has not changed since the Neanderthal days; that he remains motivated by what lies below rather than above the diaphragm; that he will always satisfy his needs by the minimum of effort; that, while capable of training, he is incapable of education because he has no wisdom and is, therefore, meat for the politician and the tyrant; that only rarely does a great soul rise above the mass, a Buddha, a Confucius, a Moses, a Plato, a Socrates, a Leonardo, a Shakespeare, a Washington, a Lincoln. The splendid list could be long. Obviously such a philosophy is vulnerable. We are not all either John Does or Emersons. There are

* Cram, Ralph Adams: Why We Do Not Behave Like Human Beings, in Convictions and Controversies.
Nock, J. A.: The Memoirs of a Superflucus Man.

all gradations between. The great leaders of medicine may not occupy the loftiest peaks with the major prophets, nevertheless, in their contributions to the welfare of mankind, Hippocrates, Vesalius, Sydenham, Virchow, Pasteur, Laennec, among the elect occupy comparable summits and give us, their humble followers, the right and the courage to speak when we sense any threat to the well-being of men or to our freedom to serve his needs.

Industrialization and urban living have divorced man from nature, divorced him from that "universall and publick manuscript" of Thomas Browne, in which we learn certain fundamental realities, cause and effect, the value of leisurely evolutionary progress, the danger of abrupt and revolutionary changes, the worth of freedom. The admitted evils of the industrial system have given rise to a demand for a new order. It is proposed that the state assume responsibility for the security of the individual from the cradle to the grave. Already we are embarked upon such a path, with little regard on the part of the mass man for the truism that security at the hands of the state and freedom as we have known and valued it are incompatible. Freedom from want and fear makes a good slogan, but will it bear analysis? Short of that degree of privation which impairs initiative and energy, are not man's wants and man's fears the common motivating forces that arouse and compel action? To be sure there are higher motives—the love of service, the wish to rise equal to one's obligations, the pride in a good job—the last seemingly lost in the assembly line of modern industry. These, alas, seem the motives of but a select few. Even in the present crisis of our country in which the impetus to selfless, devoted labor in a common cause seems required of all, has the mass man, aside from the armed forces, shown any preponderant organized tendency to act on the higher levels? Can we, overnight, by some feat of political or social legerdemain, change this attitude or elevate these motives? Again, if all fear of privation be abolished by a paternalistic government, a fear about which the individual by his own efforts can do much, has there not been substituted a more menacing fear, a fear of the state, against which no effort of the individual can avail? Must we not estimate the effect upon the mind and spirit of the mass man of the removal of his wonted mainspring of action and of the deprivation of freedom which promises to result from the assumption by the state of this power over the individual? The trend of this statism seems toward the static order

of the ant hill or the bee hive. Let those who would be drones remember that, in Nature, such are limited in number, in function, and in length of days. As physicians we already have been concerned with and concerned about some of these effects upon the individual. It is apparent that ere long we shall have to reckon with them as they affect our profession and, in consequence, the public health and welfare. To these effects the Academy cannot be indifferent.

I believe a possible result of what is called state medicine may well be a destruction of certain values of the spirit which are part of the very soul of our calling. Let us consider some of these values. "Scientific Humanism" has been declared a kind of religion, which is described further as the cult of the "sacredness of scientific progress in the promotion of the welfare of mankind." I know of no better definition of medicine than this. Whatever other faith we may profess, if this be a religion, a "*Religio medici*," if you will, it is one to which all physicians of whatsoever time, race, or nationality subscribe. No other body has achieved such universality, such catholicity; not the law, not the church. Wherever physicians meet there is unanimity of motive, purpose, method; and this has been true at all times and among all peoples. In this have we not set an example for the statesman and is there not here a value upon which the lawmaker should lay no ill-considered hand? Humanism has a twofold meaning: on the one hand it implies a sympathetic approach to one's fellow man and his problems, a sense of his needs, his inspirations, and his aspirations; it practices faith, hope, and charity: On the other hand humanism includes that which may be termed culture, a knowledge and appreciation of the stored wisdom and experience of man, as found in the "*Litterae Humaniores*" of our library, in not a few of the papers read from this rostrum, in the deliberations of our committees and in the programs of our Section on Cultural and Historical Medicine. These are no mere overtones, adding only richness of quality to professional work; they are fundamental in the symphony. Without science the physician is a menace; without humanism he is no physician. If [illegible]erforce, the physician becomes a hireling of the state, his future [illegible]ependent upon political favor, will not the humanistic side of medicine [illegible]end to shrink, perhaps even wither away?

For a moment let us be very practical. Let us note certain concrete results. A number of factors have contributed to the increased longevity

we now enjoy. None, however, has approached in importance the public and private health work, in so much of which the Academy has been a leader; often, indeed, a pioneer. Since the founding of this Academy, the life expectancy of man has increased from 35 to 63 years; that of woman fom 38 to 68 years. Can other learned callings show comparable results? In the last hundred years has the Law brought to the world more of Justice or made it easier to secure or less costly? Have legal clinics for the poor become numerous? Has Theology brought us nearer its noble goal of peace on earth, goodwill among men? Does this comparative record of medicine justify its being singled out for revolutionary methods of governmental control? Let those in other callings, whose freedom seems not as yet directly threatened, remember that encroachments by the state are progressive; that, if shackles are placed upon one group, they surely are being forged for the rest.

Life has three prime and mutually dependent values without which all else is vanity. They are the life blood of our calling and of our Academy. They are truth, justice, and freedom. If, as Emerson says, "truth is the summit; justice is its application to affairs," there are but two–truth and freedom.

I like to think of this Academy as a Temple of Truth, not of the fixed dogma professing infallibility, but of a living truth that can change with the daily revelations of science, "a streaming fountain; if her waters flow not in a perpetual progression, they sicken into a muddy pool of conformity and tradition." Is not this the kind of truth that makes man or woman free, free to live a lengthened span, free to bear and rear with little pain or risk, free to build large cities and live in them without danger of epidemics, free to explore and live in any climate, free from smallpox, plague, yellow fever, diphtheria, and many other infections, free to live and to die with little pain? In the Areopagitica we read how "Truth indeed came once into the world with her divine master and was a perfect shape most glorious to look upon" and how Typhon, the god of evil, "took the virgin Truth, hewed her lovely form into a thousand pieces and scattered them to the 4 winds. From that time ever since the sad friends of Truth, such as dare appear . . . went up and down gathering up limb by limb still as they could find them. We have not yet found them all." It is our task to join these friends of Truth and gather up some of the fragments, in our library, in our committees, in the stated and section meetings, so that, although

it may not be given to us, those who shall come after may indeed see the lovely vision of the *Virgo Intacta.*

The time calls for candid, honest and courageous leadership, a leadership based upon truth. If we of the Academy continue to give such leadership in our proper field, we shall have done all that is possible in preserving for our calling that freedom of action that has given American medicine its high standards and its effective service to the public.

This, our Academy, is a structure built by the wise and able leaders of our profession of this great city over nearly a century of effort. It is a heritage to be preserved with reverence. Let us dedicate ourselves to this work, this "Scientific Humanism" which, untrammeled, will continue to devote itself to the "sacredness of scientific progress in the promotion of human welfare."

ADDRESS OF THE RETIRING PRESIDENT*

ARTHUR F. CHACE

Two years ago when I assumed the Presidency of The New York Academy of Medicine, I pledged myself to accept the challenge of the changing world and to endeavor to lead the Academy to ever greater heights of achievement in spite of the difficulties along the path, in a world torn by a devastating war. The magnitude of the problem served as a stimulus to our best effort, for as Browning so truly said–

"But a man's reach should exceed his grasp
Or what's a heaven for."

Tonight I shall speak of the past two years in terms of my stewardship and give you a brief picture of the progress made.

The revolutionary forces in society are demanding adjustment of the public health agencies to the new order, with increasing intensity and the Academy is meeting these demands with ever-widening spheres of influence and constructive coöperation throughout its many departments.

In spite of the insufficient stacks, the impossibility of procuring foreign periodicals and the difficulty in maintaining personnel, the Library has carried on with valiant and unbroken efficiency.

In the past two years the Committee on Public Health Relations has maintained its tradition. The most important problems arising out of the war to which the Committee has given especial attention are: The progress of the treatment in Veterans' Tuberculosis Hospitals; the taking part in the national inquiry into physical fitness, the need for which was shown by the high rates of rejection among the young men called for induction into the armed forces; the standardization of the training of WACS, so as to qualify them to meet the requirements of the A.M.A. for various types of technician after their return to civil life. Among the long list of its activities the constructive recommendations improving the Workmen's Compensation System in the State, the publication of Standards on convalescent care and rehabilitation and the book on

* Delivered at the Annual Meeting of The New York Academy of Medicine, January 4, 1945.

Preventive Medicine, are most noteworthy.

At the request of the Council, the Committee on Medical Education assumed charge of the installation of a permanent drug exhibit which serves two purposes: the medical education of the physician in the newer pharmaceuticals and recognition of the contribution in research and accomplishment by the great pharmaceutical houses of this country. More than 2,000 physicians viewed the exhibit during the Fortnight period and since then the daily attendance has averaged 62 persons. The Committee has developed means to meet the expected post-war demand for post-graduate medical courses. It is preparing for an extension of post-graduate courses in independent hospitals and is giving every assistance to physicians seeking such studies. The Committee has maintained the high standards of its scientific programs with its Stated Meetings of the Academy, the Friday Afternoon Lectures, the Research Meetings and the Seventeenth Graduate Fortnight.

In all the activities of the Committee on Information there is a common denominator which is the Academy's leadership and the Academy's service to those who are concerned with the education of the public in matters of health. The Committee's projected Health Education Demonstration will have far reaching effect in guiding the in-service training of Health Educators. Educators are evincing ever greater interest in the Lectures to the Laity. In the past two years the publication of the two volumes of the March of Medicine has been enthusiastically received, as has the publication of the two volumes of the transactions of the Academy's Annual Health Education Conference. The Committee has been called upon to review and help compose a very substantial number of manuscripts, which manuscripts, dealing with important health items, are published in magazines whose individual circulation runs into the millions. The Academy, in this way, is exercising an influence which is nationwide and of major significance.

In the early part of 1943 the Committee on Medicine and the Changing Order was initiated. During the past two years it has gathered a vast amount of material and has thoroughly explored the field of social change. It has gained the support of a very substantial number of citizens from every walk of life and in every major profession. One of the twelve basic monographs which have grown out of these studies has already been published. The others are in the process of preparation. The publication of the monographs, essays and final reports will, we hope,

constitute a worthy contribution to the solution of the problem of the Changing Order.

The improvement of the Academy's economic situation during the last four years has been a gratifying achievement which made possible an urgently necessary increase in the services of the Academy. In our effort to be of service to the official and voluntary health organizations we have loaned members of our executive force to the New York Tuberculosis Association, the Welfare Council, the Navy League and the Women's Army Corps. We are happy to announce that from three sources, financial support for traveling expenses and honoraria has been obtained. The Fortnight has been permanently endowed by the generosity of Mr. R. Thornton Wilson. The Academy has aided in the recruitment and training of practical nurses. The By-Laws have been amended for the strengthening and defining of the position of the Academy with regard to medical ethics.

The pattern of man's life falls into three domains: One in which he earns his livelihood; another in which he develops cultural pursuits and the third in which he labors without thought of reward in the service of mankind. The greatness of a nation can be measured by the amount of time and effort which its citizenry devotes to such a service.

During the past two years our Fellows, in addition to their contribution to the war effort, have given more freely of their time and energy to public health, educational and socio-economic interest, not alone in this community but in ever widening circles, which reach out to the state and country as a whole. With so many of our Fellows on active war service, it is significant that those who are carrying on the work at home are serving in greater numbers than ever before in committee work. This is forcibly brought to our notice in the Director's report, which shows that 389 Academy Fellows have served in over 203 meetings. Not alone has the routine work of the committees and sections been carried forward at an increased tempo, but in the new fields of endeavor which have been initiated, all the meetings have been fully attended.

It is a source of deepest gratification to me that in the years of my stewardship I should have received unfailing support and enthusiastic coöperation from every member of the Academy family. It has been a signal honor and privilege to work with the unselfish men and women in this organization which stands for all that is best in a noble profession.

The achievements which have been enumerated have been made possible through the wisdom and statesmanship of our Director, Doctor Herbert B. Wilcox. It has been a personal tribute to his wise administration, that our splendid staff has given so unstintingly of its assistance. Through his vision the Academy has steadily grown in prestige. It is fortunate, indeed, to have a man of such administrative capacity together with such kindliness, human understanding and unprejudiced judgement.

The Academy is particularly fortunate in having as our next President, one of its Fellows who represents the highest traditions of the profession, who has had a wide experience as a clinician, diagnostician and educator and who is both a scholar and humanitarian. In following Doctor William Worthington Herrick's leadership in the years to come, I am sure that the Fellowship of the Academy will see it rise to even fuller achievement in the service of humanity.

THE TREATMENT OF BURNS AND WAR WOUNDS*

CAPTAIN L. KRAEER FERGUSON, (MC) USNR

U. S. Naval Hospital, St. Albans, Long Island, New York

THE treatment of severe burns is a problem of importance in the surgical practice of civil life, but because of their frequency in warfare, they assume a place of major importance for those handling war casualties. During a six month period in the Solomon Campaign, 364 patients with burns were treated aboard a hospital ship, which represented about 10 per cent of the battle casualties. Burns were often associated with wounds and fractures; thus of 364 patients with burns, 103 had other injuries in addition.

Burns are frequently the cause of casualties in naval battles and operations. About 84 per cent of the burns we received arose from naval actions, and of the 1229 naval casualties we received every fourth patient had a burn. These were caused by bomb or shell flash, gasoline or oil fires on ships, less often by burning oil or gasoline on the water, powder explosions, escaping steam or boiling water and occasionally by electricity. Ashore, however, most of the burns were caused by the pernicious practice of using gasoline to light fires, and less often by bomb flash or other types of enemy action. In flyers, burns were the result of both aerial battles and plane crashes.

The various burning agents produce their own types of burns. Bomb and shell explosions cause an intense heat in a short-lived flash. All covered surfaces are protected, the face and hands being burned in nearly every case. In the face, where the skin is fairly thick, the flash causes vesication and destruction of the superficial epithelium. The thinner skin of the ears, eyelids and dorsum of the hands is often completely destroyed.

Gasoline and oil fires on ships and on land and water produce more widespread burns. Clothing often catches on fire, and as a result burns involve the full thickness of the skin or all but the papillary layer.

* Read October 17, 1944 at the Seventeenth Graduate Fortnight of The New York Academy of Medicine.

Scalds from escaping steam or water may involve any portion of the body; these produce a deep destruction of the skin but usually not of the papillary layer.

Electrical burns destroy all of the skin layers and underlying tissue.

Systemic Disturbances in Patients with Burns

In the treatment of severe burns, the problem is not only that of treating the burned area. The real problem is rather one of treating a patient whose physiologic processes have been markedly disturbed by a burn. This concept is fundamental because it turns attention from the relatively unimportant dressing of the burned area to the extremely serious and often fatal systemic alterations that occur with burns.

Shock. Of these disturbances, shock is the first and most serious. It is believed to account for 60 to 75 per cent of the fatalities in burned patients and for practically all of the deaths that occur in the first two or three days after the burn is received. In our experience, its development and severity has depended more on the surface area involved than on the depth of the burn. Burns of certain parts of the body, as the face, abdomen and genitalia, perhaps produce shock more rapidly than burns of other areas.

The mechanism of the development of burn shock is a combination of factors acting in sequence. The first is a psychic one and it includes pain, fright, apprehension and frantic overexertion which goes with the production of the burn. In severe burns, especially where the burning continues over a period of time, as when clothes catch on fire or a survivor is surrounded by burning oil or gasoline on the water, this factor alone may be enough to cause fatal shock. It varies somewhat with the temperament of the patient. This type of shock is commonly classified as psychic or primary shock.

Secondary shock, which closely follows and even overlaps the phase of primary shock, is brought about by an increased capillary permeability resulting in a rapid loss of fluid from the circulation.

The increase in capillary permeability is the result of several factors. Of first importance is the effect of heat on the tissues. Kabat and Hedin[1] have shown experimentally that sensory impulses from the burned area play a role in the production of increased capillary permeability. As fluid loss leads to more marked hemoconcentration, oxygen transport is less efficient, and it is probable that anoxia brings about an

increase of capillary permeability in parts of the body away from the burned area.

This fluid loss has been termed by Koch[2] "white hemorrhage" because it really is a loss of the blood volume by a seeping of blood plasma from the vessels into the tissues in the burn area. A relatively small amount of fluid is lost in blister fluid and on the burn surface. Most of the loss is into the tissues in and for some distance around the burn. The fluid loss begins at the time of the burn and increases progressively at an unbelievable rate. It is probable that most of the loss occurs in the first six hours, but it continues for at least 48 hours and probably longer. The amount of fluid lost may be amazing. Blalock[3] has shown experimentally that it may equal 50 per cent of the blood volume in an animal with a burn involving half of the body surface.

Toxemia. The period of shock, which may be considered to last for the first 3 or 4 days after the burn, gradually merges into a period of toxemia characterized by fever, albuminuria, hematuria and at times by delirium and vomiting. Absorption of toxic breakdown products of burned tissue, is held by some to be important in producing the symptoms of toxemia. In large part, however, it is due to infection. Since burns are primarily sterile by reason of the mode of causation, infection must be looked upon as secondary. It may arise as the result of contamination from the nose, throat or hands of attendant personnel, or from unsterile dressings or clothing. Infection may become apparent about the fourth or fifth day, and is a threat until complete healing of the burned area takes place. It is frequently the factor that produces additional destruction of the skin cells with consequent delayed healing. When bacterial invasion occurs, metastatic abscesses may appear in parts of the body distant from the burn, so that infection must be looked upon as a most serious complication and the one which most often produces fatalities in the later stages of the burn.

The toxemic phase in severe burns is further complicated by the loss of the excretory function of the skin, renal insufficiency and a gradually increasing secondary anemia. As time goes on, the patient grows weaker and there is a loss of vascular tone leading to edema, thrombosis and embolism.

Treatment of Systemic Disturbances

A consideration of this brief summary of the physiologic changes

associated with severe burns leads logically to a plan of treatment designed to overcome or prevent them. The psychic shock at the time of the burn cannot be prevented, but the continued pain and apprehension may in large measure be relieved by adequate sedation with morphine given at the earliest opportunity. The Navy supplies morphine in syrettes, and usually an initial dose of ½ grain was given. Subsequent doses of ¼ grain were given as needed.

Fluid loss may be partially prevented by the early application of pressure dressings. This principle, first suggested by Koch, has been of great value in our experience. In burns of the extremities, elastic bandages were applied over the definitive dressing on the burn area. In burns of the trunk, a scultetus binder was used to provide pressure.

There is some evidence that the use of adrenal cortical extract (eschatin) may reduce capillary permeability and so prevent fluid loss. In a few cases, we gave 5 to 10 cc. doses intravenously every 6 hours for 2 to 3 days as suggested by Rhoads, Wolff and Lee.[4] This may be an accessory agent of some value but should not be relied upon to prevent fluid loss in severe burns.

The most direct and effective means of overcoming fluid loss is by replacement with plasma. Plasma was available to us in adequate amounts in packages so that one unit of 250 cc. corresponded to the plasma removed from 500 cc. of blood. In estimating the amount of plasma needed we found the formula of Black[5] most convenient and accurate enough for clinical use aboard ship when numbers of burns were being treated. His formula,

$$\frac{\text{Hb. after burn}}{\text{Hb. before burn}} = \frac{5000 \text{ cc.}}{5000 \text{ cc.} - x}$$

X = Plasma loss or plasma needed in cc.

assumes that the hemoglobin after the burn bears the same relationship to the normal hemoglobin as the normal blood volume does to the blood volume after the loss of fluid caused by the burn. We assumed a normal hemoglobin of 95 per cent and solved the equation for various levels of hemoglobin, making the following table for convenient estimation of plasma dosage.

Hemoglobin	Plasma dose
95	250 cc. (1 unit)
100	500 cc. (2 units)
105	750 cc. (3 units)
110	1000 cc. (4 units)
115	1500 cc. (6 units)
120	1750 cc. (7 units)
125	2000 cc. (8 units)
130	2250 cc. (9 units)

Hemoglobin estimations were made every six hours during the first two days and we were thus able to follow the fluid needs of the patients fairly accurately and to give plasma as needed. Of course, if large amounts of fluids were taken by mouth, this method of estimation was not so accurate as at first, but it served as a reasonably useful and practicable clinical guide. Harkin's rule of giving 100 cc. of plasma for every point above 45 in the hematocritic reading is not feasible aboard ships, because hematocrits are not usually available, and in treating burns in large numbers it is not practicable. Berkow's[6] method of estimating the extent of the burn is helpful when a more accurate method is not at hand, but it is not too exact when plasma replacement must be done on this basis. In using this method, it is recommended that 1000 cc. of plasma be given if 10 per cent of the body surface is burned, 2000 cc. of plasma if 20 per cent is burned, and so forth, surface area estimates being trunk 38 per cent, lower extremities 39 per cent, upper extremities 18 per cent, and head 6 per cent.

It is important to have some way of estimating the plasma loss, because the tendency is to give too little rather than too much. In almost any severe burn, it is safe to give at least 500 cc. of plasma (2 units) at once. We have given as much as 2,500 cc. of plasma and 1,500 cc. of saline in the first 23 hours after a burn.

The shock phase of burn therapy should not be passed without commenting upon the use and abuse of heat in this connection. Experimental evidence and clinical experience has shown that heat is no longer to be considered an effective means of treating shock. This is just as true in the care of burn shock as it is for traumatic shock. Overheating in a shock tent produces sweating and an unnecessary fluid loss in an already depleted patient. We tried to make the patients' environmental temper-

ature one of comfort, using covers or heat cradle as the case indicated, but making no effort to apply any additional external heat.

Although infection is probably the most important factor in the toxemia of burns, its consideration may logically be held over until the discussion of the care of the burned area. Adequate fluid intake should be maintained, either by mouth or intravenously if vomiting occurs. Hemoglobin estimations usually show a rapidly developing anemia which demands repeated transfusions.

The Treatment of the Burned Area

The care of the burned area should be considered of secondary importance except in so far as it helps in the prevention and treatment of the shock, toxemia and sepsis of the patient. Much can be done locally, however, to influence the systemic effect of the burn.

To begin with, those treating the burned patient should do everything possible to prevent contamination of the burned area. This means wearing masks and maintaining, as far as possible, a sterile technique in caring for burns. To avoid further shock, no attempt should be made to do any more than is absolutely necessary to clean up the burned area. Our practice was to remove loose bits of burned tissue and the raised surface of blebs and blisters as carefully as possible with scissors and forceps. As a prophylaxis against infection, a sulfonamide was used locally. We have preferred sulfathiazole in micro-crystalline form because it is absorbed more slowly and lasts longer (3 to 4 days) on the burned area. It may be sprayed on with an atomizer to cover large burned surfaces rapidly, or applied as a 3 to 5 per cent water-soluble ointment. Sterile gauze is then applied in generous layers and over this a firm pressure bandage. The elastic cotton webbing bandage does very well for this purpose, and it should be applied always to include the hand or foot distal to a burned extremity. To obtain even pressure on irregular surfaces such as the hand, sterile cotton waste was used underneath the bandage. In cases where burns were associated with wounds or fractures, plaster casts were often used as pressure dressings with good results.

Early dressings should be applied with the idea that no further dressings will be necessary until the burn is healed. Frequent dressing of burned areas accomplishes nothing except to open avenues for contamination to enter. Most second and superficial third-degree burns will

completely heal without infection in 10 to 14 days if the dressings are not disturbed. A leakage of serum through the dressing may call for a local re-enforcement but not a complete change of the primary dressing.

In third-degree burns with deep destruction of the skin but preservation of the papillary layer, the liquefaction necrosis of the destroyed skin is often mistaken for infection with pus when it appears on the dressings at about the end of the first week. The change of dressing is best delayed until the 10th to the 14th day, at which time much of the slough will have separated and can be removed by saline irrigations and mechanical removal with forceps and scissors. The burn is then redressed with sulfathiazole powder spray and pressure as before. This is repeated as necessary until healing occurs. Unless there is complete destruction of the skin, most burns will heal with this method of therapy without clinical evidence of infection. When there has been complete destruction of the skin layer, healing can occur only by the ingrowth of epithelium from the skin edges. This results in a prolonged period of painful dressings with much scarring and marked debility. Early skin grafting as soon as a suitable granulating base is apparent, permits rapid healing with a minimal scar, and it avoids the loss of weight and strength that otherwise occurs.

In the local care of burns, the objective to be achieved is a dressing that provides protection against contamination and against injury to surviving cells, a measure of bacteriostasis and pressure. It appeared to us that a dressing performed with sterile precaution, with the application of sulfathiazole and pressure, more nearly fulfilled these requirements than any other.

Tannic acid has been abandoned because it has been shown to destroy surviving cells, it sooner or later cracks and so permits infection to occur in the sloughing tissue, and it does not provide pressure except in circular burns where it may so constrict as to produce marked peripheral edema. Paraffin wax spray has the same faults except that it does not coagulate surviving cells. The triple-dye treatment is unsuitable in severe burns for the same reasons.

In severe burns, patients occasionally lose weight and strength rapidly in spite of repeated transfusions and other supportive measures. This is often associated with a loss of vasomotor tone, thromboses and a gradually increasing debility and asthenia. We tried to counteract

these changes by getting patients out of bed early, at first letting them sit in a chair for a time and, as soon as possible, getting them up on their feet, this in spite of fever and toxemia. It seemed to us that this was worthwhile and we have seen no untoward reactions.

In 364 patients with burns, at least half of which could be classed as severe, we had one death due to burns alone. One patient died of multiple wounds, compound fractures of both bones of the lower leg and burns received in a plane crash. One other patient with multiple injuries and burns died soon after leaving the ship. It seemed to us that the death in these two latter cases was in large measure due to their other injuries. Most patients were comfortable within a few hours after their definitive dressing, and healing progressed rapidly. One patient with more than 75 per cent of his body surface burned by live steam recovered with only minor skin grafting.

The Care of Battle Wounds

The incidence of wounds in battle varies a great deal with the type of military operation so the figures on war wounds vary from theater to theater. Our experience aboard a hospital ship gave the following statistics. In a six months period beginning with the amphibious landings at Guadalcanal and ending after the Japanese had been driven from that island, 6,807 patients were received aboard, of whom 3,333 were surgical casualties. (These figures represent only patients received aboard the ship from the battle area, but do not by any means represent the total casualties of the area.) The patients were divided 1,229 Navy, 1,589 Marines, and 509 Army, this representing a fair cross section of both naval and land casualties.

Types of Wounds

The casualties arising from naval actions were usually produced by aerial bomb or naval shell fragments, or by injuries received from mine or torpedo explosions. About one in every four naval patients had burns. In land battles about half the casualties arose from bomb, shell, mortar or grenade fragments, and the other half from machine gun or rifle or pistol bullets.

Almost all wounds produced by explosion fragments were classified as shrapnel wounds. These varied in size from large wounds with much loss of tissue to small peppering wounds. They were usually multiple

and appeared in several areas of the body. In wounds from naval shells there was also a local burn caused by the red hot shell fragment.

Bullet wounds were more often single and often through and through. When the bullet passed through soft parts without encountering bone only a small tract of injury was made. When bone was struck, however, the deflection of the bullet caused a large wound of exit with a considerable tearing of soft tissues. There was a relatively large number of through and through wounds of the buttocks. These occurred due to the fact that the buttocks were often the highest point of the body as the soldier or marine crawled through the brush in land actions.

In the three thousand odd casualties, 2644 had open wounds, not counting the burns. By far the majority of the wounds were of the extremities, about 67 per cent. Wounds of the head and face 6.8 per cent, chest 7.4 per cent, abdomen 2 per cent. The latter figure does not give a true picture of the number of intraperitoneal injuries, however, because many wounds of the back, loin, buttocks and perineum caused intraperitoneal damage.

Principles of Wound Care

In anticipation of the handling of battle casualties, we had formulated some principles on which to base our treatment. Briefly these could be outlined, as follows:

(a) Measures to control hemorrhage and to obtain hemostasis.

(b) The removal of dead, devitalized and contaminated tissue, and of foreign bodies. Under this head we had visualized the necessity of debridement.

(c) The prevention of infection. Under this heading in addition to the mechanical removal of contaminated tissue, we had added the local and systemic use of the sulfonamides.

(d) The avoidance of further injury. No antiseptics, gentle handling of tissues.

(e) Physiological rest, by the use of immobilizing dressings, splints or casts.

(f) Preservation of an adequate arterial circulation. Prevention of edema by elevation and pressure. Sympathetic block in cases of traumatic vascular spasm, the use of cold to reduce the local metabolism in cases of borderline vascular supply.

The care of wounds in warfare, however, requires some modifications of previously held ideas as to how to handle the injuries arising from trauma. There is no change in the principles of wound care, but there is required some thought as to how these principles are to be applied in view of new and strange conditions, varied facilities, multiplicity of injuries, numbers of casualties, and the necessity for moving the patients with a consequent succession of surgeons treating a wounded man.

Our first casualties came aboard seven days after they had been injured. Most of the patients had had little more than emergency treatment, which consisted of sulfanilamide or sulfathiazole powder in the wound and a battle dressing, many had had sulfathiazole or sulfadiazine by mouth. It was surprising to note the relatively low incidence of signs of inflammation in spite of extensive wounds. There was, of course, some sloughing due to the trauma of the injuring agent. It appeared to us that these cases were received too late for debridement, and, therefore, a conservative plan of treatment was decided upon. The patients were taken to the operating room. The doctor and two or three corpsmen scrubbed and dressed as for operation, and anesthesia was given (usually spinal anesthesia for lower extremity or lower abdominal wounds, and intravenous pentothal for other wounds that could not be handled by local anesthesia). The wound itself was protected by sterile gauze and a thorough mechanical scrubbing of the skin of the entire area was carried out, using large quantities of soap and water. After the skin surrounding the wound had been cleansed, the wound itself was exposed and thoroughly irrigated with saline solution. We had available sterilized enema cans, to the tubing of which a large sized catheter was attached and used as a nozzle. During the irrigation of the wound, such loose tissue as floated away in the irrigating solution was excised with scissors and forceps. We removed foreign bodies that were easily accessible in the wound and bone fragments which had no attachment to periosteum or muscle. An effort was made not to produce bleeding in this cleansing process, and no attempt was made to excise the wound or wound tissues. In cases in which a small wound was overlying a large, deep pocket, the incision was extended to make it correspond to the underlying wound. As experience was gained in the handling of these wounds, it was found that it was not necessary to remove caked sulfanilamide from an open wound as it came away with

the slough and necrosis or disappeared with time. In a few cases, it was necessary to partially remove the caked drug as it acted as a plug in the mouth of the wound.

After this conservative cleansing of the wound, microcrystalline sulfathiazole in the form of a powder was sprayed on superficial wounds, or it was introduced in an aqueous suspension in deeper wounds. In most wounds, a simple gauze dressing was applied with a considerable amount of pressure to prevent edema in the wound area or to disperse it if it was present. All large wounds of the extremities were immobilized with plaster splints or casts. When the patient was taken to the operating room, it was our purpose to give in that treatment and dressing the definite wound care. Unless it was necessary because of excessive secretions, the wounds were not dressed again during the patients' stay on the ship. Most of our patients left the ship before the end result of their treatment could be determined, but it was possible for us to follow these cases in the hospitals to which we had evacuated them and in a few instances we were privileged to carry the patients along until complete healing had occurred. This enabled us to evaluate somewhat our conservative form of therapy. It was evident that the wounds became clean and free of slough within a period of 10 days to 3 weeks after injury, and at that time it was found possible to perform a secondary suture in a large percentage of the cases. Even relatively large wounds could be completely closed if skin excision had not been carried out. In other cases, it was possible to close wounds partially by suture, reducing, therefore, by one-half or more the area which had to be covered by skin graft.

Such excellent results seemed to follow our regimen of mechanical cleansing, immobilization, pressure dressings and sulfathiazole locally in patients who came to us relatively late, that we were encouraged to follow the same regimen in early cases. It appeared to us that by the early local and systemic use of the sulfonamides there was little necessity for wound excision or extensive debridement.

We received aboard the ship numerous patients upon whom so-called debridement had been performed. This usually meant excision of the wounds with removal of all damaged tissue and loose bone fragments. The resulting wounds were much larger than the original wounds. No secondary suture was possible and frequently the convalescence and healing in these patients was prolonged.

No attempt at suture of battle wounds was made while patients were aboard our ship. However, we received a fairly large group of patients in whom suture had been attempted from the second to as late as the sixth day after injury. In tabulating these patients, we found that in 190 of these wounds sutures were successful, if one counts as successful wounds showing serum ooze, slight hematoma, and slight redness around the suture line. The majority of these wounds were small originally, less than 3 cm. in length. We found that these wounds healed without suture in approximately 2 to 3 weeks. In 157 sutured wounds the entire wound had to be opened because of infection, hematoma, or necrosis. These usually were large wounds in which a debridement and suture had been attempted.

There were certain types of wounds, however, in which wound suture seemed practicable. Wounds of the face especially fell into this category. In our group, we had 35 facial wounds, of which 31 were successfully sutured. It is fortunate that wounds involving the face and mouth can be sutured successfully almost any time after their inception because these patients have not only to contend with the pain of the wound, but they have also a marked psychological disturbance because of fear of disfigurement; and in mouth wounds, they have marked dehydration and malnutrition due to the difficulty of eating and drinking. Some of our most grateful patients were those in whom suture of facial wounds was successful. Wounds of the scalp not involving the underlying bone or brain could also be sutured successfully in many cases. Eleven out of 16 scalp wounds healed primarily without infection even though they were sutured late. In our experience, wounds did poorly when they were associated with compound fractures in which suture and application of a cast had been performed. Some of our most severe infections appeared in such cases.

Foreign Bodies

Foreign bodies of all sizes and shapes were found, and they varied in number from 1 to 50. It was impossible to consider removal of all foreign bodies by operation, and it was found by experience that a great many of them could be picked out of the wound with forceps or hemostat without anesthesia. As the injured tissues became necrotic, foreign bodies frequently worked to the surface or could easily be reached through the wound.

Some indications had to be laid down for the removal of foreign bodies, and as experience grew these indications became more definite:

1. Those which were easily accessible in the wounds were removed at the time of wound cleansing.

2. Those which were superficial were removed by a simple skin incision.

3. Those which, because of their size or position, caused interference with function, thus all foreign bodies in the joints were removed when possible. Large foreign bodies in soft tissues were removed.

4. Those which, because of position, caused pressure on vital structures, thus foreign bodies which pressed upon the trachea, upon the nerves, etc., were removed.

5. Those which developed infection around them were removed, and in these cases the removal of the foreign body accompanied the incision and drainage of the infected area.

6. Those which worried the patient because of their presence were removed.

Patients were often upset by the knowledge that their tissues contained shell fragments in a certain area, and wished them to be removed. The rule was that no foreign body should be removed in which the procedure of removal would cause more damage than the presence of the foreign body in the tissues. Most of the foreign bodies could be removed under local anesthesia; relatively few of them showed any infection about them and in most cases after the application of sulfathiazole into the wound, the wound edges could be loosely brought together with 1 or 2 wire sutures.

Fractures

Fractures occurred in 1,285 of 3,333 battle casualties. More than one of every three patients had a fracture, and 46 per cent of the patients with wounds and contusions, or almost every other patient, had a fracture. Fractures were observed in almost every bone of the body. There were certain characteristics of fractures in military surgery that became apparent at once. The fractures often involved more than one bone and more than one part of the body; as typical examples were patients with fractures of both femurs and a radius, femurs and both tibias, dislocation of the shoulder and fractures of the clavicle, 4 ribs and the os calcis of both feet. The second characteristic was that most fractures were

compound. Of the 1,285 fractures, 1,062 or 83.6 per cent, were compound. A third characteristic was the fact that most of the fractures were shatter fractures with marked fragmentation of the bone, but without much displacement. Often only one of two bones was broken.

The problems of fracture care in battle casualties aboard the Hospital Ship were varied. First, and perhaps most important, was the care of the wound, and in compound fractures wound care did not differ from that described for other wounds. Secondly, the patient had to be immobilized so that he could be moved painlessly from shore to ship and from ship to shore, and, if necessary, at a moment's notice to lifeboats or liferafts. It was apparent then that no form of traction which necessitated weights or pulleys could be used. Therefore, all fractures were treated in plaster, often with the addition of skeletal fixation by means of pins or Kirschner wires. Plaster immobilization was adopted for the further reason that traction was out of the question because of the movement of the ship and because of the number of cases. During one period there were aboard 22 patients with compound fractures of the femur.

Internal fixation was used in only 4 cases. In two patients screws were applied to fix fractures of the epicondyles and in two cases of fractures of the forearm plates were applied. In none of these was the wound sutured. The Roger Anderson apparatus was available for use throughout the entire period in which casualties were being received. It was used in only two cases.

Unpadded casts were used in the care of fracture cases. Felt pads were placed to protect bony prominences and vaseline was applied over the skin to prevent the hair from sticking to the plaster. No form of padding was used, however. In a few cases it was necessary to split the cast after it was applied, and in all cases the circulation was carefully watched, but no complications arose from the use of unpadded plaster casts in our hands. In order to preserve the cast in patients whose large wounds produced profuse drainage, it was necessary to make windows over the wounds so that absorbent dressings could be changed as required. Although this took away some of the advantages of the closed plaster method, it seemed the lesser of two evils, otherwise the casts had to be changed because of softening in a matter of 2 or 3 days.

Chest Wounds

Chest wounds represented 7.4 per cent of the total wound group,

but only about half of these showed intrathoracic injury. It was evident that the chest cage protected the patient against intrathoracic trauma in many of the wounds resulting from low velocity missiles. Through and through wounds of the chest were not uncommon from bullets, and it was surprising to note the relatively little intrapulmonary damage that was produced in these cases. Even the presence of intrathoracic foreign bodies produced few clinical or X-ray findings.

Fractures of the ribs and scapula were quite commonly associated with chest wounds. In patients with hemothorax it was found that the pain and fever were increased by repeated tappings so that it became our policy to reserve this procedure for those cases in which there was dyspnea or in which infection was suspected. Sucking wounds were not common and in most cases they were treated by packing and in only one case was suture performed.

Wounds of the Abdomen

Wounds of the abdomen represented 2 per cent of the wound group, but it must be remembered that wounds of the loin, back, and perineum also frequently produced intraperitoneal injuries. All of the patients who came to us had been operated upon before they reached our hands. It became apparent from observation of these cases that suture of the wounds of the stomach and small gut gave a much better prognosis than those of the large gut. Many of the patients in whom intraperitoneal injuries resulted from wounds received from the back, had large retroperitoneal hematomas which appeared to do well without drainage. Most of the abdominal wounds which were sutured after operations upon the large gut became infected and broke down; hence it seemed to us that no effort should be made to close the skin and subcutaneous tissues in these cases, and we recommended suturing the muscle and fascia with stainless steel wire and wound packing following the application of sulfathiazole locally.

Vascular Injuries

In the treatment of battle casualties with large wounds, secondary hemorrhage not infrequently occurred. We rapidly learned to be constantly on the lookout for this complication so that immediate treatment could be given. Hemorrhage occurred in 13 cases, in 8 of which it was necessary to take the patient to the operating room for a liga-

tion of the bleeding vessel. Another vascular injury which was observed in 10 cases was pulsating hematoma. This was seen most often in the thigh, but occurred also in the neck, arm, forearm, and lower leg. Because of a severe hemorrhage which occurred in our first group of patients, we afterwards performed ligation and excision of the injured artery and vein in such cases. These operations were performed on the average from 8 to 10 days after injury. In our group of cases there were 5 of the femoral artery, one of the brachial artery, and one of the radial artery. In none of the cases was there any evidence of any peripheral arterial difficulty following ligation.

Gas Gangrene

Aboard the Hospital Ship, 10 cases of clinical gas gangrene, proved by culture, were seen. Of these, 5 died and 5 lived. Two of the deaths occurred two and one-half and five hours after the patients came aboard the ship and one death arose from gas infection that appeared in the stump of a patient who had an amputation performed before he arrived on the ship. Of the other two deaths, one occurred following a mid-thigh amputation of the lower leg where gas gangrene was already present, and the other 12 days after injury in a patient whose thigh wounds had been sutured the day of his injury. Gas gangrene occurred in the muscles of the thigh and lower abdomen, and in spite of the wide incision and intensive treatment, death occurred on the third day after admission to the ship.

Gas gangrene as seen in the South Pacific occurred exclusively in casualties from land battles. It occurred in 1.0 per cent of 3,333 casualties, but it was the cause of about half of the mortality in these 3,000 patients. It was characterized by a tension type of pain without the production of much gas in the tissues. In several of our patients, gas was not demonstrable in the X-ray. There was not the characteristic discoloration of the skin, or at least this discoloration was not recognized when associated with ecchymosis and swelling. Temperatures varied between 100° and 102°, and the most characteristic laboratory finding, aside from culture, was a very high leukocytosis, which ranged between 20,000 and 40,000. At operation, the tissues presented marked edema and the typical brick red coloration.

In the treatment of gas gangrene, conservatism again was practiced. In those patients in whom there was an evident disturbance of the

blood supply to the part, a guillotine type amputation was performed, and for this operation refrigeration was the anesthesia of choice. During the two hour period of refrigeration all absorption from the infected area is effectively blocked by the tourniquet, and this time may be well used to give supportive and specific treatment. Where there was an adequate blood supply, wide incision was practiced with the local and systemic use of sulfathiazole, immobilization of the part, and huge doses of gas gangrene antitoxin (100,000 to 200,000 units in 24 hours intramuscularly). In our series, this was the method of treatment used for the five patients with gas gangrene who lived.

X-ray was not used as a method of treatment of gas gangrene because the X-ray machines available were not suitable. Penicillin was not available to us at the time. It may be that the use of this therapeutic agent will improve results in this type of infection.

Since returning to the States, penicillin became available as an agent to combat infection in war wounds. We have had an experience with it in a large variety of cases and have seen its almost miraculous results. It has been used both locally and intramuscularly in the late treatment of infected wounds. It is apparent that neither the sulfonamides nor penicillin are any substitute for good surgery. The same surgical principles still hold. Adequate drainage has to be provided, sequestra have to be removed in the same way as before these drugs were available. On the other hand, by controlling infection with penicillin and the sulfa drugs surgical procedures may often be successfully attempted which would have been impossible without their use.

No discussion of the treatment of war wounds would be complete without some mention of the systemic treatment of the wounded man.

The use of plasma in generous quantities and its availability in the front line aid stations has been the most outstanding advance in the treatment of shock in battle wounded. This, combined with morphine and rest, are therapeutic measures that have proved their value.

In many patients plasma administration must be looked upon as a stop-gap until whole blood can be given to replace that lost due to wounds. Little resistance to infection or healing of wounds can be expected in patients with hemoglobin readings of 40 or 50 per cent. We had a living blood bank in the crew of our ship and transfusions were given in liberal quantities until the hemoglobin was 70 per cent or over.

Bed rest, quiet and good food are three other therapeutic measures that aid in the rapid recovery from war wounds. These can only be had outside the battle zone, hence the value of rapid transportation via air or ship to areas of relative safety.

It is apparent that war wounds are not much different from wounds of civil life except that there are more of them. The surgeon who cares for them should remember the dictum of Paracelsus—"Every surgeon should know that it is not he, but nature who heals. The physician is but the helper, who furnishes nature with weapons. The apothecary is but the smith who forges them. The business of the physician is therefore to give nature what she needs for her battle." What I have told you tonight is an example of one effort to solve the riddle of giving nature what she needs in her battle for war wounded.

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THE REACTIONS OF TISSUES FOLLOWING INFECTION AND THEIR PLACE IN AN ENVIRONMENTAL CONCEPTION OF THE NATURE OF DISEASE*

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WHEN Doctor Jaffe invited me to take part in this centenary meeting of The New York Pathological Society and to share in the program of The New York Academy's Graduate Fortnight, I was greatly pleased. Merely to have been invited was sufficient reason for this; but there were other considerations: In the first place, here was presented an opportunity to meet a group of pathologists, only a few of whom I could call personal acquaintances; in the second place, the occasion offered an enviable opportunity to discuss one of my major interests with a group of critical colleagues; in the third place, your Graduate Fortnight is one of the few occasions on which pathologists are recognized for what they really are, students of disease, and are brought together with their clinical colleagues to acquire through the medium of critical reviews a more intimate knowledge of current problems in the science of medicine.

I do not flatter myself by thinking that I can announce to a company of this sort a new set of general pathological principles which underlie the reactions of tissues to infectious agents. Through great familiarity with disease processes, you all know too well those few essential biological responses to stimulation which characterize mammalian tissues to expect such a thing of me. Nevertheless, through a reëxamination of certain ones of our well known pathological principles, and thus, through the exposition of a certain point of view, somewhat novel though that point of view may seem to you, perhaps I can pay you at least in part for the nice compliment which you have paid me through your invitation to this meeting.

* Read before the Centenary Meeting of the New York Pathological Society in connection with the Seventeenth Graduate Fortnight of The New York Academy of Medicine, October 19, 1944.

During the past fortnight, you have heard interesting and instructive accounts of the progress which is being made in the study of certain practical aspects of infectious disease. You have had reviewed for you those really amazing procedures that have been developed for the control and, indeed, the cure of such plagues as gonorrhea, pneumonia, syphilis, and certain meningococcal and streptococcal infections; perhaps, even the arch enemy of the young, acute rheumatic fever, may be included in this list. These accomplishments have come through the hard thinking and drudging labor of colleagues who no longer put their trust in empiricism and favorable accident, but who, instead, build according to plans and specifications dictated by established basic biological principles. In the discussion you have heard, the emphasis, by plan, has been placed on the practical and, indeed, timely problem of the *specific treatment of specific disease entities* produced, as we are accustomed to say, by *specific etiological agents*. Under a bombardment of this sort, particularly in the face of the urgencies of the times, it is natural to think of disease almost solely in terms of the *specific living things* which we say *cause* disease and in terms of the *specific dose of poison*, so to speak, which we may administer to those living things to dispatch them. Biblically speaking, our chief objective for the moment has come to be the casting out of the parasitic devils! In normal times, when there is no insistent O. S. R. D. and thinking and working is more deliberate, there is less tendency to forget that, though the earth and the firmaments may be asquirm with the seen and the unseen living agents of disease, *where there is no host for these potential parasites there can be no disease*. And so, there is some purpose, and perhaps momentary relief, in having discussed for you at the conclusion of this fortnight that most important factor in infectious disease, the host.

The one who would attempt to understand disease has his attitude towards its problems determined well in advance by his conception of the basic nature of disease. Since what I propose to say regarding tissue reactions in infectious disease is in the nature of an attempt to understand disease, it is necessary for me to lay before you my own conception of the nature of disease before going forward with the development of the main theme which has been selected for this presentation.

I have been able to find no broader attitude toward the problems of general biology, a branch of which medicine surely is, than that expressed by Claude Bernard; he has put the matter this way:

> *"As the essence of things must always remain unknown, we can learn only relations, and phenomena are merely the result of relations."*

Being confident that this great man's mind penetrated to the core of things biological, I have been quite willing to accept his view that we can learn only relations and so have formulated my own conception of disease as follows: *Disease is a matter of the abnormal outcome of a constantly changing relation between the ultimate biological unit, the cell, and its environment.*

This environmental conception of disease is comprehensive enough to permit emphasis wherever it may be appropriate. It is sufficiently restrictive to enforce proper consideration of all the factors which enter into the relationship. It permits of no dissociation of injury and reaction to injury, and it makes of etiology and pathogenesis an entity which cannot be disrupted without destruction of the whole concept.

Lest some of you become a bit impatient with this seemingly impractical consideration of the matter, let me show you how this concept of disease may be applied to that large group of important infectious diseases characterized by the invasion of the body by the viruses. Nobody questions the existence and the etiological significance of certain substances now identified with some of the more typical diseases that belong to this group and called viruses; and yet, with one or two exceptions, we know virtually nothing about most of these substances except what we have learned by studying the *relation* between them and the host cell. We identify them in almost every instance by studying *not the virus* but *the reactions of the host cells to the virus*, that is, the host-parasite relationship. Improvements in techniques may make it possible in the future to study the physico-chemical constitution of all of the viruses isolated in highly purified states, as already has been accomplished with a few of them, but this would not guarantee us a better understanding of the diseases to which they are related. A crystalline virus in a test tube is indeed an import[illegible]ttle cosmic unit, but that intratestubal relationship is very different from the obligate cell-parasite relationship which comes into being when a virus characteristically takes up its residence within a living cell. In the diseases produced by these agents, the physical and biological relationship that exists between the virus and the host cell is so intimate and so mutually essential that, in one's thinking, there is no possibility of divorcing the agent from the

cell; therefore, the study of both the virus and the disease caused by the virus turns out to be nothing other than the study of the outcome of a very intimate and complex intracellular host-parasite environmental relationship. Under these circumstances, it is only natural in considering the nature of the viral diseases to place the emphasis upon the reaction of the host cell rather than upon the virus which provokes that reaction.

Having been impressed by the greater importance of the cell reactions in the viral diseases, I have thought that it would be profitable to look into the matter of the host-parasite relationship which obtains in the common bacterial diseases to determine whether or not a comparable situation exists in these infections. Wherever I have turned for materials for study of the problem the outcome has been the same. My own continuous study of ever recurring human and animal infections, the studies of experimental infections carried out in my own laboratories and in the laboratories of many colleagues, the critical reviews of others who have interested themselves in the problem and the investigations of workers in the basic biological sciences, all, have been found to point in the same direction: In the final analysis, it seems that the greatest advantage is gained by using the reaction potentialities of the cell as the keystone in the building of a satisfactory conception of disease.

Some of our clinical colleagues, I am sure, will not accept this emphasis without vigorous protest; and their protest has a right to be heard. They, like we, know that we cannot breed disease-resisting strains of human beings as the intelligent farmer breeds his cattle and his corn. They know that they must accept man as they find him. They know from many trials and errors that what little they may undertake to do in the way of changing the basic reaction potentialities of the tissues often turns out badly. It, therefore, appears to them to be more practical to give first consideration to the extrinsic etiologic factors in disease causation. It is not difficult to join in these protests because experience has shown that at least in a few instances it is possible to prevent disease simply by eliminating the parasite from the environment of the potential host. In some instances it is even possible to destroy the parasite within its host. Along with our clinical colleagues, we might be content to enjoy that chronic optimism which their successes with the prevention and treatment of a few of the more spectacular infectious diseases pro-

vides if it were not for that large group of diseases that bedevil us during the last half of our three score years and ten. Our almost complete helplessness in the face of these diseases is sobering, to say the least; we need no more potent stimulant than that offered by this helplessness for a more thoughtful consideration of those internal factors in disease causation which, for the moment, we may call the reaction potential of the cell.

As we shall see presently, no parasitic infection is a simple killing matter such as is the blow of the guillotine knife. Whatever the parasite may be, the disease produced by it is a time-consuming process. That which takes place as time runs on—hours, days, months, or years as the case may be—as I see it, is determined almost solely by the cellular reactivity of the host. As far as I can find out, there are no fundamental changes that take place in the parasite during parasitic disease; the invader remains essentially as it was the day it entered the tissues *except in so far as it may be altered by the reactions of the host tissues.*

If tissue reactivity in disease is as important as I have attempted to make it out to be, a definitive description of this reactivity should be presented before proceeding further; otherwise, the whole discussion might degenerate into a mere metaphysical exercise. This I shall try to do for you briefly.

Admittedly with some danger of over simplification, I have found it useful to view the reaction potential of cells and tissues as follows: When cells or tissues are injured they may react in four essential ways:

1. They may submit more or less passively to the injury and thus go through the process of dying and disintegrating.

2. They may react in such a way that they protect themselves and other tissues against further injury, thus playing a sort of automatic defensive role.

3. Under certain conditions of injury they may become so adapted through alterations in their functions and structure that they effect a compensatory adjustment for losses of function by other related tissues and thus make it possible for the individual of which they are a part to remain in comparative equilibrium with its environment.

4. They may undergo a basic alteration in their reactivity which makes them more highly susceptible to injury by a given agent than they originally were.

At once it will be apparent to you that the submissive and the de-

fensive reactions of tissues are most apt to occur immediately following injury; they usually take place in the presence of the specific agent producing the injury. The reaction of adaptation may be immediate and direct, but, in its most impressive form, it is a secondary phenomenon which takes place after a primary injury in an entirely different but related tissue has occurred. The hypertrophy of the heart muscle which results from the increased work requirement created by an injured and incompetent valve is a good example of this. The reaction of sensitization takes place only under rather specialized conditions of injury, and it is dependent upon actual contact of the cell with the injurious agent; its complete development is always delayed.

Here a word of caution is necessary. In any given pathological situation one may find all four of these basic reaction types represented. As a rule, however, one of them dominates the situation and thus gives a certain character to the disease entity in connection with which it occurs. Because of this, it is possible and, as I see it, quite useful to classify our common disease entities on the basis of the prominence of one or another of the basic reaction types which characterize these entities.

In order that this discussion may be brought into more proper reference to the occasion I shall now do three things. First, I shall focus your attention upon the environmental relationship which exists between the cell and the surrounding fluids in an area of injury by bacteria; this will serve the double purpose of emphasizing the importance of the environmental conception of disease processes and of bringing into relief a few of the more interesting types of cellular reaction. Second, I shall make a few pertinent comments on the somewhat peculiar reactions of certain tissues which are becoming more and more prominent as the most probable basis of some of our least-well-understood diseases. Finally I shall make a few comments on the nature and classification of infectious diseases especially as determined by the basic reactivity of the tissues.

In infectious disease, opportunity is presented for the study of reactions which involve all kinds of cells; those most conspicuously implicated are determined by the extent of the invasion of the infectious agent. At the site of entry of infectious agents and at all points of subsequent localization, an environmental situation develops which gives rise to all the basic forms of cellular reaction. The total effect of these

reactions may be considered to be resistive and hence, with reference to the individual, defensive. We call this situation inflammation. It will serve our purposes to examine this environmental situation with some care. In so doing, however, we need not undertake a consideration of all the important aspects of this vital response of the tissue to injury.

The presence of an infectious agent in the tissues changes the local environmental relationships in one or more of three essential ways. First, it alters the fluid medium in which the cell must live; second, it may give rise to a specific alteration in the basic reactivity of the cell; third, it may change the cytoplasmic and nuclear structural and functional constitution of the cell. A few illustrations will help to clarify what I mean.

First, let us examine the environmental situation which develops when a type III pneumococcus is introduced into the tissues of a rabbit. This animal, as you may recall, usually is not seriously harmed by this organism, although a sharp local reaction is provoked. In the animal which possesses only its natural resistance to injury by this organism, the pneumococcus finds in the fluid environment of the host cells all its metabolic requirements, and, within the first few hours, it is relatively undisturbed in its propagation and spread. The relatively unrestrained growth of the organism quickly alters the character of the intercellular fluids in a profound way. Not only do the living organisms discharge their products of metabolism into these fluids, but also those organisms which do not survive disintegrate and contribute their own basic chemical substance to the environment. Since the basic metabolic requirements of bacteria and cells are the same, the living organisms create a local cellular nutritional imbalance by competing with the living cells for the nutriments available in the common environment. Important changes occur also in such factors of the fluid medium as the ionic concentration, osmotic pressure, hydrogen ion concentration, viscosity, *et cetera;* and, what is additionally significant, these changes may involve all the circulating fluids of the host. This change in environment is incompatible with the normal functions, even the life, of both the fixed tissue cells and the freely wandering cells of the fluid and tissues. This being particularly true of the capillary endothelium, the environment becomes further altered by the excessive transference of fluids to the tissue spaces and, indeed, by the extravasation of whole blood. Up to this point the pneumococcus has had its own way with the exception

of a restriction of its spread from the area of primary injury through the action of certain mechanisms of natural resistance the details of which need not concern us at this point. But, this local change in environmental relationships has its general effects. The rabbit develops a temperature elevation, and, if the experimental evidence does not mislead us,[1] therein lies the undoing of the pneumococcus. The new local environmental situation created by the temperature elevation makes it impossible for the pneumococcus to continue to produce its capsules. These unprotected organisms then become the victims of leukocytes whose normal phagocytic activities previously had been thwarted by the barrier which the capsular substance offers to phagocytosis. Thus, it appears that a change in a single factor of the environment of the cell results in a complete reversal of the cell-bacterium relationship, and the infection quickly comes to an end.

Infection of a rabbit with a virulent type I pneumococcus provides an excellent opportunity to study another type of alteration in the environmental relationship of cells, one which involves an entirely different set of factors from that just discussed. If this organism be introduced into the skin of a non-immune rabbit, the animal develops a bacteriemia within a few hours and dies. If the tissues at the site of inoculation are studied histologically, it will be found[1] that the organisms spread rapidly and diffusely through the tissues as they proliferate and that they produce grave injury to the tissues. Phagocytosis of the organisms is minimal. In animals previously exposed to pneumococcus I infection or passively immunized, the situation is very different. Histologic study of the tissues of these animals reveals a localization of the bacteria and a tendency of the organisms to grow in clumps. Furthermore, there is active phagocytosis of the organisms by the reacting leukocytes. It is obvious that the immunized animals are effectively protected because they survive the infection. We know that this is accomplished by adding something to the cellular environment which not only facilitates phagocytosis but also brings about clumping and restraint of spread of the growing organisms. [There appears to be no interference with the growth and propagation of the bacteria except that referable to phagocytosis and digestion by the leukocytes. This is indicated by the fact that immunized animals deprived of their leukocytes die of the infection just as do the non-immune animals.[1]] This alteration in the fluid environment of the cells appears to be the result of a specialized

form of cellular activity, that is, specific antibody production. [We do not know just what cells are concerned in this alteration of the environmental fluids, but we are assured that those at the site of infection are not solely responsible.[2]]

In the preceding paragraphs, emphasis has been placed upon some of those changes which take place in the fluid surrounding the cell that are responsible for an alteration in the cell-bacterium equilibrium. It was pointed out that some of the changes are referable to the bacterium and some to the reacting cells. Next, I shall discuss the second way in which entry of bacteria into the tissues gives rise to significant disturbance in the environmental relationships of the tissues; this consists of the stimulation of a specific alteration of the basic reactivity of the cell, and it may or may not result in the *addition* of something to the environmental fluid. As you may surmise, I refer to the development of what we call tissue sensitization.

It is necessary at this point to recall that there are two types of tissue sensitization that arise in the course of bacterial infection. These differ in what appear to be fundamental ways. I refer to a) anaphylactic sensitization, with which may be included that type of cellular alteration which underlies the Arthus phenomenon, and b) bacterial allergic sensitization, the best known example of which is that out of which arises the tuberculin reaction. Zinsser[3] was the first to emphasize the differences between these types of sensitization. Rich, in his recent monograph on the pathogenesis of tuberculosis,[4] has outlined the matter in his Table XVIII which I have taken the liberty to reproduce (Table I). For our immediate purposes we need refer to only one of the differentiating features cited in this table, that which relates to the blood serum or, more specifically speaking, to the medium surrounding the cells. In the case of anaphylactic and Arthus sensitization, the fluid environment of the cells is altered by the *addition of antibody* just as it is in the case of immunization of the rabbit to the pneumococcus cited above. As a result, the environmental relationship thus set up by the infection may be transferred from an infected animal to an uninfected one, and when the cells of the latter are subjected to contact with the specific antigen they react quite like the cells of the former. This situation does not prevail in the case of bacterial allergic sensitization. The alteration in the environmental relationship which occurs in this form of sensitization is referable to a change in the basic reaction potentiality of the host cell

TABLE I

THE CHARACTERISTICS OF THE TYPES OF HYPERSENSITIVITY

Illustrating the similarities of the anaphylactic, Arthus and pollen types, and their differences from the tuberculin type.

			Type of Hypersensitivity			
			Arthus	*Anaphylactic*	*Pollen*	*Tuberculin*
Usual *minimum* requirement for establishment of sensitivity.	Single parenteral contact with small amount of free antigen		0	+	+?	0*
	Parenteral contact with repeated small amounts, or with a single large amount, of free antigen		+	0	0	0
	Parenteral contact with intact bacteria or virus		0	0	0	+*
Some of the clinical effects that may result from contact of the previously sensitized body with the specific antigen	Prompt local oedema, erythema, foll. by haemorrhage, inflammation, necrosis		+	0	0	0
	Prompt, evanescent, local oedema and erythema		+‡	+	+	0
	Generalized oedema		+	+	+	0
	Generalized urticaria		+	+	+	0
	Symptoms of asthma (dysp.) or hay fever (nas. fulness; lacrymation)		+	+	+	0
	Prompt, fatal anaphylactic shock		+	+	+	0
	Prompt, non-fatal constitutional reaction		+	+	+	0
	Delayed constitutional reaction, fatal or non-fatal		0	0	0	+
	Delayed and prolonged local inflammation, and necrosis.		0	0	0	+
Evidence for site of action of antigen in sensitized body	Action directly on extravascular tissue cells	Necrosis of cells on contact with antigen *in vitro* (tissue culture)	0	0	0	+
		Necrosis of cells in avascular tissue *in vivo* (cornea)	0	0	0?†	+
	Action on capillaries	Increased capillary permeability (local oedema)	+	+	+	+
		Necrosis of capillaries with haemorrhage	+	0	0	+
	Action on involuntary muscle	Spasmodic contraction of involuntary muscle *in vivo* and *in vitro* (Dale bath)	+	+	+?†	0
Body sensitized to a bacterial protein reacts hypersensitively to the intact bacteria			0	0	—	+
Passive transfer of sensitivity readily accomplished.			+	+	+	0

* See text for possible exceptions.
† Not tested.
‡ With small dose of antigen.

which involves factors that are inseparable from the cell body. It is especially interesting to note that in certain types of bacterial allergic sensitization (tuberculin sensitization) the sensitized cells will grow and reproduce themselves in normal serum *(in vitro)* and transmit their sensitivity to their daughter cells.[5] This would seem to indicate a genuine constitutional alteration of the cell in the course of allergic sensitization. We are reminded, in this connection, of the constitutional factors that appear to be almost regularly involved in the sensitization of bronchial asthma, and of certain food allergies. It is the stimulation of these anaphylactic and bacterial allergic reactivities of the cell that I wish to call attention to as the second previously cited mechanism through which the invasion of the body by bacteria changes the environmental relationship within the tissues. Reference to the accompanying table will show how important the environmental situation created by hypersensitivity is, especially as it may influence the reactivity of the endothelium and smooth muscle, that is the vascular system.

I have cited for you some of the essential changes that may take place in the environmental relationships of the cell following the entry of bacteria into the tissues particularly as they relate to the composition of the environmental fluids and to the basic reactivity of the cell and have suggested to you some of the significant effects of these environmental changes. For the sake of completeness, a few words should be said relative to the changes that may occur in the environmental relationships through alterations in the structural and functional constitution of the cell which are not immunological. My point in this connection can be made most effectively by reference to the viral and the rickettsial infections.

In the viral and rickettsial diseases we deal with an extraordinary form of parasitism which has as its chief characteristic the intracellular residence of the parasite. Properly to understand these infections it is necessary for one to carry the environmental concept quite beyond the level of the cell and to think in terms of the relation between the physico-chemical constitution of the nucleus and the cytoplasm of the cell as it may be related to the physico-chemical structure of the particular agent concerned. I have no intention of entering into a discussion of this problem for the very simple reason that I know very little about it. Nevertheless, by way of illustrating my point, I can cite for you the most important alterations in cellular reactivity that arise out of the

disturbance in the intracellular environmental situation that is created by the invasion of the cell by, for example, a virus. Briefly they are (1) increase in reproductive activity resulting in an extraordinary hyperplasia, (2) alteration of the metabolism of the cell in the course of which specific antibody is produced, (3) profound alteration in the basic growth potentiality of the cell resulting in a condition indistinguishable from genuine anaplasia, (4) death and disintegration of the cell.

For our clinical colleagues there is an important practical consideration involved in this matter of intracellular cell-parasite relationship. We are all familiar with the ineffectiveness of the treatment of the viral and rickettsial diseases by our new chemotherapeutic substances, the sulfa drugs and penicillin. It is not improbable that the very striking difference between the effects of these agents upon the bacterial and the viral and rickettsial diseases is due in part to the fact that in the latter the therapeutic agent may never reach the parasite for which it is intended; or, perhaps, it reaches a parasite which is doubly protected from the drug, first by the surface constitution of the parasite itself and, second, by the barrier of cytoplasmic or nuclear protein which surrounds the parasite.

Passing now from a consideration of the environmental relationships of cells as they may be altered by the entry of infectious agents into the tissues and the potential changes in basic cellular reactivity that result from these environmental alterations, I shall next say a word or two about the somewhat peculiar reactions of certain tissues which appear to be particularly susceptible to alterations in their reactivity when the environmental relationships become disturbed by infection. These tissues are the blood vessels and the connective tissue. I select these tissues for two reasons: In the first place, they are concerned importantly in practically all forms of inflammation *immediately* resulting from invasion by infectious agents and, in the second place, changes in the reactivity of these tissues play an essential role in certain delayed manifestations of infection the full significance of which is only just now coming to be widely appreciated.

I can make my point with regard to the reactions in the blood vessels that are directly and immediately incident to the invasion of the tissues by infectious agents by very brief statements. The vascular aspects of the inflammatory reaction are too familiar to every one to require more consideration. The essential vascular reactions relate to

the endothelium and to the nerve-muscle structure. The results of these reactions are an increase in permeability of the endothelium to all the components of the blood—including, it may be emphasized, circulating antibody—accompanied, if not actually preceded, by a marked dilatation of the vessels. Injury of the endothelium is followed by thrombosis and circulatory obstruction, and death of vascular muscle and connective tissue results in hemorrhage. These reactions, which are essentially submissive, are followed by a marked proliferation of endothelium, connective tissue and even muscle (the formation of granulation tissue), essentially a compensatory process. All of these reactions and their importance are so familiar to you that nothing more need be said about them.

Connective tissue we recognize to be the common clay, the filler, or the matrix of body structure, but, even so, it is composed of potentially the most highly reactive cells that go into the structure of the body. Because of this, connective tissue almost always is involved wherever tissues react to injury. Only the immediately killing injuries can take place without provoking a literally speaking "reactive" response on the part of connective tissue cells. The two most common reactions of connective tissue cells are the two extremes, proliferation and death and disintegration. A consideration of both of these reactions can be used profitably in the further development of our theme.

In all destructive injuries to tissue, the local cellular relationships become quite complex; in this, fibroblasts are conspicuously involved. Let us consider for a moment the situation which arises in the course of the formation of a simple bacterial abscess. At the margin of this lesion, a proliferation of fibroblasts occurs and continues, so to speak, so long as there is *need* of these cells for the reëstablishment of the continuity of the tissues. I realize that the conception of *need* as a stimulant for the proliferation of tissue cells is an annoying abstraction, but I know no other way of putting the matter since nobody really knows why these cells proliferate. The only at all satisfactory reason for the growth of the connective tissue cells is a very general one, namely, that there exists locally an environmental situation involving a variety of factors which makes a change in the spatial, structural and functional relationships of the surviving cells necessary if tissue equilibrium is to be reëstablished—that is, if the lesion is to heal. [All of this adjustment takes place quite automatically; therefore, just because the word *need*

has been used in this connnection, it is not necessary to become disturbed by the conventional fears of a teleological influence creeping into our conception of tissue reaction.]

My chief reasons for selecting this particular reaction of the connective tissue for discussion is that it provides an opportunity for me to comment upon the environmental relationship represented by the encapsulation of an infected focus by fibrous tissue proliferation. It is generally said that the body protects itself against infection by the encapsulation or "walling off" of the infected area by newly produced fibrous tissue; a fibrous capsule about an abscess, thus, is said to constitute an effective barrier to the further development and spread of the infection. As I see it, the capsule of fibrous tissue is there not because of a *need for protection of the tissue*, but because the other genuinely defensive mechanisms (phagocytosis, natural immunity, et cetera) have operated so effectively that the invaders are restrained and eventually destroyed, thus creating a new local environmental situation which in its turn constitutes a *need* of an entirely different sort from that just mentioned, *a need for the restitution of the local tissue equilibrium.* This is met through the proliferation of fibroblasts at a far greater rate than is the rate of destruction of these cells; the result is the encapsulating fibrous membrane. The formation of the capsule of an abscess, thus, is merely the expression of healing of the lesion and, therefore, is nothing more or less than the formation of a scar. As far as I know, there is no indication that scar tissue is particularly resistant to destruction by bacterial action.

In the preceding comments on fibrous tissue reactions accompanying infection, the emphasis has been placed upon local tissue relationships which result either in fibroblastic proliferation and fibrosis or in death of connective tissue cells. A far more interesting relationship involving connective tissue reactions following infection and related processes is that out of which arises a slow and even sublethal degenerative (sometimes quite dramatically and acutely necrotizing) reaction of the connective tissue, particularly the reaction of the collagen fibers. I refer to that peculiar change in the mature connective tissue, chiefly that in the blood vessels, in the endocardium and in the membranes lining and adjacent to the joint cavities which we know as *fibrinoid or hyaline degeneration.* We know ever so little about the environmental situation which gives rise to this reaction, but its effects are quite familiar to us.

The whole matter is a live issue just now and has been for the past two decades. The more we learn about it the more apparent it becomes that we must go back to the early studies on the phenomenon of tissue sensitization to get our leads to its understanding. To follow the thread of argument in support of this view of the matter is not possible at this time, so I shall ask that you be content for the moment with the suggestion of the basic idea and permit me to proceed to the concluding part of this discussion.

What remains for me to say chiefly consists of a comment on a group of disease entities underlying which, we now have good reasons to believe, is an environmental situation characterized by varying degrees of tissue sensitization to proteins, some of which surely are *bacterial* in origin.

I have devoted the bulk of what I can say regarding the reactions of tissues following infection to those reactions which can be dealt with best at the level of the cell. Since, after all, there are very important practical considerations involved in the study of disease that relate to the summation and integration of all the cellular reactions, that is to the individual reacting as a whole, it will be useful to say a few words about types of infectious disease as they are determined by the reactivity of the tissues arising out of infection.

Basing our ideas upon the reaction potential of the tissues in the face of infectious agents, it is possible to see the infectious diseases as falling naturally into two groups as follows:

Group I: Diseases in which the conspicuous tissue reaction is *direct and immediate* following the invasion of the infectious agent through what we all know as acute or chronic suppurative and chronic granulomatous inflammation. Good examples of these are pneumonia, peritonitis, purulent meningitis, and primary tuberculosis.

Group II: Diseases in which the reactions of the tissues to the infectious agents are *indirect and often if not characteristically delayed.* These diseases are chiefly the result of the submissive (alterative or degenerative) type of reaction of the tissues to injury. The typical injurious agent is an initially non-toxic chemical substance derived from the infectious agent which becomes highly toxic as a result of the development of tissue sensitization. To this group of diseases, we have good reasons to believe, belong certain types of bronchial asthma, acute rheumatic fever, periarteritis nodosa, acute and chronic diffuse glomeru-

lonephritis, certain types of chronic arthritis, and (perhaps) lupus erythematosum disseminatum. Certain forms of tuberculosis, perhaps chronic brucellosis, some of the mycoses, and some of the other genuinely granulomatous diseases, with some justification, might be included in this group.

I shall not bother you with any further reference to the disease entities which fall into Group I since the problems of pathogenesis they present are not novel, though many of them are far from adequate solution. Nor do I think it profitable to review the essential problems in the pathogenesis of those diseases of Group II which are more or less accepted as examples of bacterial sensitization. Instead, I wish to leave with you the suggestion that in the principles involved in the pathogenesis of those diseases now accepted as arising out of the cellular environmental situation created by bacterial allergic and anaphylactic sensitization we *may* have the key to the understanding of some of those disease entities which still defy pathogenic analysis. Outstanding among these is a group of so-called *degenerative* diseases. The feature common to all of these is a necrotizing disintegration, sometimes very slow and sometimes even explosive, of the connective tissue and its embryologically closely related substance, smooth muscle. This, in some of its several histologic forms, resembles strikingly the fibrinoid or hyaline degeneration that is so characteristic of those diseases which we have good reason to believe are related to bacterial or other types of sensitization. The diseases referred to are (1) eclampsia, (2) bilateral massive cortical necrosis of the kidneys, (3) medionecrosis aortae idiopathica, and (4) the sphinx of all the so-called degenerative diseases, arteriosclerosis.

In what I have had to say to you, my chief objective has been to lay before you a point of view. Since a point of view is after all an abstraction, and abstractions are never easy things to deal with, with the hope of giving the point of view in question some semblance of concreteness, I should like to reduce the matter to a schematic representation for you. The environmental relationship out of which disease arises is represented in the accompanying drawing.[6] The diagram represents a complex individual separated from the great unlimited *external environment* by a living zone of exchange. In the center is the ultimate biological unit, a living cell, which is surrounded by a complex but limited *internal environment*. The prevailing condition is the state of health characterized by an equilibrium between the factors of the internal

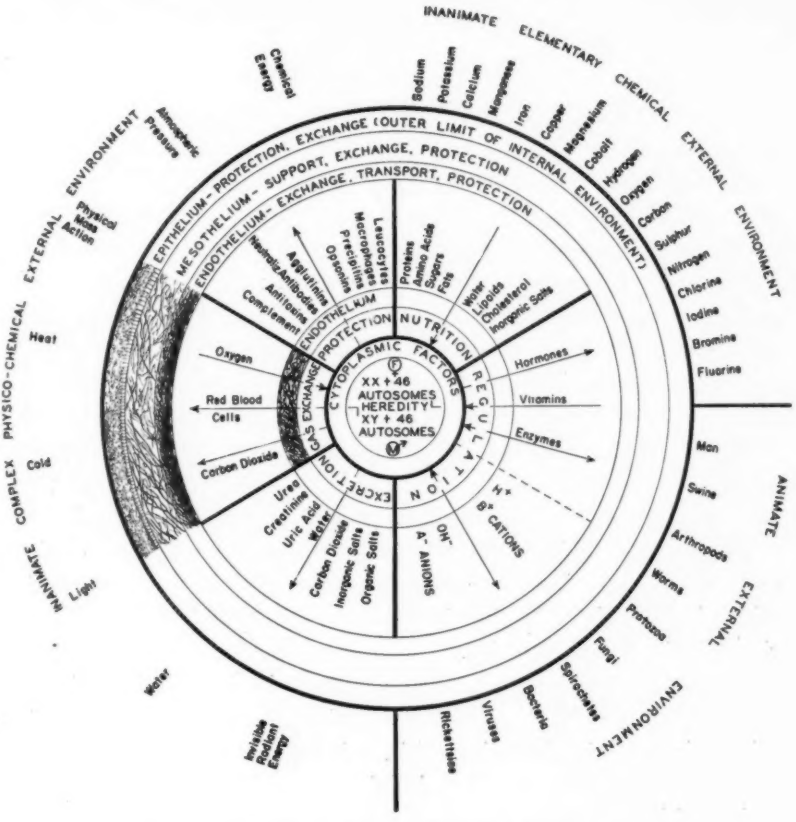

Fig. 1—Reactions of tissues following infections, etc.

environment and the factors of the external environment.

Beginning at the periphery and passing to the center of the drawing, the concentrically arranged zones and what they represent are as follows: (1) The external environment, the unlimited outer universe.—In this zone exists the animate and inanimate factors concerned in health and disease. The relative importance of the external environmental factors in the health equilibrium is presented roughly by the length of the corresponding segments of the circumference. (2) The outer zone of the exchange between the individual and the external environment.—In this zone are included the two outer, limited, concentric areas in which reside certain important factors that influence the rela-

tion between the individual and the outer world, namely, protection, support and exchange. These factors are represented anatomically by the epithelial and mesothelial tissues. (3) The inner zone of exchange between the individual and the external environment.—This zone is the area between the two concentric, shaded circles designated "endothelium." In this area are the continuously circulating fluids which surround the cell. Physically and chemically speaking, this is the internal environment of the cell, which represents the simplified individual. The factors which reside in this zone are many, but they all fall into five major groups, excretion, regulation, etc., as indicated. The physical and chemical components of this internal zone of exchange originate either in the individual, that is, in the cell, or in the external environment, as indicated by the arrow points. (4) The innermost zone represents the simplified individual, the cell.—This zone is bounded by the black circle which represents the cell membrane; within this is the innermost circle, which represents the cell nucleus. In this innermost zone resides the ultimate factor which determines the balance between the individual and the outer environment; this factor is the individual constitution, which is determined by the chromosomal and cytoplasmic make-up of the cell, that is, by heredity.

In concluding, I should like to state again the point of view the presentation of which has been the main objective of my discussion: Disease is not a simple killing affair. It is a matter of the abnormal outcome of a constantly changing, infinitely complex relation between the ultimate biological unit, the cell, and its environment; and, by corollary, the etiology of disease, more specifically speaking, infectious disease, is not *an organism,* but is *a relationship between an organism and a cell.*

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* The author will furnish a complete bibliography upon request.

LIBRARY NOTES

*MEDICAL LIBRARIES AND MEDICAL HISTORY**

GERTRUDE L. ANNAN

Medical libraries play an important role in the history of medicine, for the library has always been the parent of historical study. Through the library the records of the past have been preserved and historical research made possible. Through the library such study has been fostered and stimulated. In earlier days only those who made scholarship their career had the leisure and the necessary background, while in the cloistered halls with manuscripts chained to desks, welcome was accorded to a privileged few. The introduction of printing, the publication of texts in the vernacular, the vast increase in the number and size of libraries, has made historical study available to everyone.

Time, however, is even now an obstacle to all but the professional historian, and it is as much a problem to most medical librarians as it is to the busy physician. Few can spare more than a fraction of their time away from the pressure of current or routine duties. Yet for the library to play its proper part, time of both medical man and librarian must be consumed. Only through such coöperation can their aims be realized.

In the building of a collection of books, it is with the advice of those who are to use them that the librarian can achieve the best results. Every library, large and small, indicates in its holdings a line of development, but this must be coördinated with the needs of its readers. Every want can of course not be satisfied, but each suggestion is welcomed and considered. The physician interested in the history of his specialty can better determine the value of a contribution to it, while the librarian in reading secondhand book catalogues can bring to his attention desirable items offered for sale which might be wanted for his personal library. Through such joint assistance competition may be avoided and the librarian will not duplicate volumes expected at a future date to be presented to the library.

The physician, too, can help the librarian in a plea for the preservation of the memorabilia often carelessly hidden away in homes of the families or descendents of physicians. These, the records of today, will be as valuable to the historians of this era as the documents of past centuries are to those of earlier periods. Too often correspondence, minutes of medical organizations, documents, diaries, announcements and advertisements of seemingly ephemeral interest, have been discarded or relegated to musty attics. The historian realizes that the most unimportant item may have utmost value to the writer of tomorrow, and it should be the responsibility of both librarian and physician to publicize the necessity of preserving such records and depositing them in the library. The paper salvage drive has unfortunately swallowed up much that should have long since been rescued, but there must be more remaining to reward the efforts of the persistent. Important, too, is the attitude of the librarian toward proffered gifts. The Academy Library recently received extremely interesting autograph letters of important medical men of the early nineteenth century

* Read before a joint meeting of the New York Society for Medical History and The Section of Historical and Cultural Medicine, on November 8th, 1944.

because a university librarian to whom they had first been offered was not properly appreciative. The only possible excuse for not welcoming donations of that kind is the constant problem of every library, lack of space. But surely no additional space will be granted until the urgency of the need is overwhelmingly obvious. There are gifts, of course, that would be out of place in a collection, but a suggestion of a more appropriate depository would convince the donor that the rejection was not based upon a lack of interest, and more fitting offers might be forthcoming.

No medical man of the past is so obscure, no book, pamphlet, or document so worthless that they merit oblivion. Too many of our predecessors were not of this opinion, much to the loss of the libraries. One who saw into the future more wisely than most of his contemporaries was the patron of the Academy Library, Dr. Samuel Smith Purple. On our shelves are hundreds of bound volumes of pamphlets which he saved from destruction. These include many American medical theses, a large number published before 1800, contributions by Samuel Bard which are of some rarity today, articles by Samuel Latham, Mitchill, Benjamin Rush, David Ramsay, Charles Caldwell and others, besides eighteenth and early nineteenth century tracts by English writers.

I would like to quote from an address delivered by Dr. Purple before the Academy in 1877.[1] His words may be familiar to some of you, but surely they bear repeating.

"A popular error exists in the profession, and it has done much to retard the establishment of a good reference medical library in this city. There are not a few who believe that only the best books and latest editions are worth preserving. This idea has tended greatly to retard the growth of our own Library during even the past two years. No book or pamphlet is worthless; every waif from the mental laboratory of the practical physician contains a fact, or, it may be a statement of facts, which, however darkly concealed or obscured by peculiarities of language or description, will ultimately be unearthed, and serve the genius of practical medicine or medical history. In illustration of the truth of this statement, witness the recent disclosure which your speaker made, first in the Section on Obstetrics and the Diseases of Women and Children, and afterward in this Academy, that more than a century since, Drs. Colden and Bard described here epidemics of diphtheria—the scourge of our city in these days.

"The description of this disease by Dr. Cobden, in 1753, lies concealed in a somewhat scarce and neglected publication of a long since extinct medical society of London; whilst the description of the epidemic of this disease in this city, in 1770, by Dr. Samuel Bard, is contained in this little brochure which your speaker rescued from the press-box of a second-hand paper-dealer in this city *in transitu* to the maw of a paper-mill. Its former owner had sold it for the eighth part of a cent, or at the rate of two cents per pound . . .

"Will any Fellow of this Academy, from this time forward, despise the day of small things, or consign to collectors of rags or paper stock the pamphlets, or old editions of medical works, which he may weed from his library or garret? Will not all bear in constant remembrance that here, in this our own Medical Home, will be gratefully received and carefully treasured every tract, pamphlet, book, manuscript, engraving, portrait, small or great, which may be donated?"

The Academy Library cannot show gratitude enough to Dr. Purple. His efforts in salvaging medical material are not his only contribution. His library, which included 5,900 volumes of American medical journals, was bequeathed to the Academy and served as the nucleus of the collection. His notations, sometimes in separate manuscripts, are of great use to us today. One volume is consulted frequently by those interested either in the first years of the Academy or in the New York medical men of that period. On each page is the name of a founder of the Academy. In Dr. Pur-

[1] Purple, S. S. *Medical libraries* . . . New York, 1877, pp. 18-19, 25-26.

ple's hand are brief biographical notes, references to obituaries or other biographical sketches, and occasionally newspaper clippings containing obituaries. Some give scanty information, but may cite the only record we possess of the men in question. Other of his manuscripts include biographies of well known physicians, a short bibliography of American doctors and their writings, a bibliographical account of the medical periodical literature of the United States, a chronological list of medical periodicals in his own library covering the years 1797 to 1857, and a list of organizing members and Presidents and Vice-Presidents of the Medical Society of the State of New York.

Few physicians today have Dr. Purple's leisure or his devotion to the world of books, but the far reaching effects of his services to this Library can indicate to those interested in medical libraries or medical history, paths along which they might choose to follow.

The building of a useful collection, is of course only half the battle. The value of any collection can be judged solely by its use, and since the number actively interested in the history of medicine is small, the resources of the library of medical history are seldom fully utilized. The library can play a large part in stimulating the study of history, although discouragement may often be the reward. Statesmen, economists, lawyers, military strategists, must have knowledge of the history of their professions, but the majority of scientists feel that only the new is worthy of attention. A few years ago an editorial in the bulletin of an English hospital noted that a recent gift was the only book on the history of medicine in the hospital library and remarked that it would be well to add a few more of the standard works and to introduce a few lectures on the subject. This mild suggestion provoked an immediate response in which the writer inveighed against investing "time and energy in a subject that did not give a profitable return." He said, "There can be no possible use in knowing anything about Bright or Addison or Lugol, nor in any of the dilettante frills that so please those who possess them."[2] This attitude is unfortunately shared by many, and the librarian who meets it frequently must wonder just how much time may be spared for such "dilettante frills," and how far he should go in trying to arouse interest in them.

It is obvious that those who are strongly against historical study are not apt to be influenced by any efforts in that direction, but there are those who, although they favor having an historical collection, feel that old volumes are merely curios or museum pieces, relics of an ignorant past. These and the medical students make up the audience that might be swayed, might profit by having historical material brought to their attention. As in advertising, "eye appeal" is surely the most successful bait. The man who passes unheeding by the carefully prepared exhibit which took hours of study and research, will pause before a small display arranged in a prominent spot with suitable illustrations and not too much text. New accessions may be shown, or descriptions of them mimeographed and circulated, such as Dr. McDaniel's informative and delightful "Fugitive leaves." Recent gifts should receive proper publicity. Reprints of articles by members of the organization may awaken the interest of their colleagues. Accounts of the activities of other organizations may also provide incentive. Dr. Sigerist in his report of the activities of the Institute of the History of Medicine for 1943/44, describes their exhibits for that year. He lists three types: the scientific exhibits; the monthly student exhibits which correlated the history of medicine with current events, through such subjects as Salerno in medicine, Sicily in medicine, etc.; and the book of the week exhibits which showed either a new book of particular interest, a new accession, or a publication of a member of the faculty. Every librarian cannot find the time for such a varied program, but surely some effort can be made in that direction.

The real work of the librarian, however, should begin with the new enthusiast.

[2] *St. Thomas hospital gazette*, 1940, vol. 38, pp. 59, 121.

Whether medical student or practising physician, the novice in the field of history is in need of assistance which the librarian can easily supply. The casual student may be satisfied with a few readable volumes. The serious student, and there will never be many, must go on from there. The first thing he must learn is the importance of original sources. He must be taught to consult them whenever they are available. He must be made to realize that no historian is infallible; that no source but the original is to be relied upon; that every fact must be documented; that every bibliographical reference must be clear, complete and specific, citing author, title, imprint, volume and page. Above all he must learn the necessity of accuracy. Dr. Sarton writes, "The main point to emphasize . . . is that accuracy is as fundamental in the historical field as in the scientific one, and that it has the same meaning in both fields . . . Most of the historical work done by scientists untrained as historians is published without means of verification, that is, with insufficient or imperfect references, and with so little accuracy that it is useless for later scholars . . . Such work is obviously a waste of time for all concerned. It can add nothing to our knowledge."[3] Dr. Sarton does not add that later scholars may not be the only sufferers, for the historian himself may at a future date wish to check his sources. Then he must retrace his steps, a difficult and time-consuming chore after a lapse of time.

The next step for the beginner is to become familiar with the necessary reference tools. Here, too, the librarian can render the utmost service. For a rich heritage awaits the medical historian. History, biography, bibliography. In each field medical men have left enduring monuments. No subject has been more thoroughly covered. In the field of bibliography it is outstanding. In fact, the father of bibliography was a physician. The handsome folios containing Conrad Gessner's extraordinary work were published in 1545 and 1548. Today they stand upon our shelves, not alone as a tribute to Gessner's industry, but also as useful books of reference. The *Bibliotheca universalis*, covering all existing literature, is no simple list of authors and titles, but an annotated catalogue often giving brief biographical notes, detailed contents, quotations from the authors' prefaces, the imprint, the number of chapters, and the source of his information. He may indicate that a volume was noted in Champier's *De scriptoribus medicinae* or in Tritheim's *Catalogus ecclesiasticorum scriptorum*, or he may mention the particular library in which he examined a copy of the book in question. Bibliographers of today can look with awe upon this tremendous compilation.

Gessner was succeeded by medical men of equal industry who confined their attention to the subject of medicine. Manget who brought out many large volumes in the early eighteenth century often quoted extensively from the original texts. Haller later in the century cited obscure texts and scarce editions overlooked by other bibliographers. Ploucquet in 1793-9 provided an extensive index of medical literature by subject, including references to case histories in the sixteenth century *Consilia* and to articles in the early scientific journals. In the years 1830 to 1845 appeared a thirty-three volume catalogue of recent medical publications, arranged by author and compiled by the Danish physician, Callisen.

These are but the most outstanding achievements in medical bibliography. There are many others over the centuries which make contributions to the subject. Together they comprise a vast amount of valuable material, material which has necessarily lost some of its glory in the shade of the work most vital to any medical library, the *Index-Catalogue*. Billings may be remembered as the last of the giants of medical bibliography, for through his efforts and those of his successors at the Army Medical Library no one need embark upon the impossible task of listing the ever increasing and voluminous mass of medical literature. Today bibliographers can limit

[3] Sarton, G.A.L., *The study of the history of science*, Cambridge, Mass., 1936, pp. 10-11, 46.

themselves to subjects of less general scope, such as the detailed descriptions of editions of the writings of one author, so well exemplified in the books by Dr. Keynes, Dr. Fulton and Miss Doe, or of one specific subject, such as Schmid's bibliography of pathological anatomy.

Medical history and biography have been no less well served. As Dr. Malloch has pointed out[4], it is only when the medical historian investigates subjects outside his particular field that he can appreciate the vast bibliographical and historical resources of his own. The novice may well be bemused and bewildered when he is faced with this literature for the first time, and the librarian is needed to show the way. Obviously no catalogue, however detailed, can offer adequate descriptions. The catalogue must be supplemented by the librarian's familiarity with the contents of his collection, by his intimate knowledge of the value of different volumes and by his imagination, a quality which should never be underestimated in historical research. Imagination and persistence are the most necessary qualities for both librarian and historian. Imagination can direct them to the less obvious sources where the needed information may lurk unsuspected. Persistence spurs them on when the discouragement of unsuccessful search fails to turn up a small but important detail. For the true historian realizes that history is but the amassing of one small fact after another, dull perhaps to the facile interpreter who is satisfied to base his calculations upon the work of others. But the historian knows that the discovery of any fact, no matter how insignificant, is an indisputable contribution. He knows, too, that the pursuit of such a fact may entail a chase as interesting as that of a detective in search of a criminal or the hunter in search of his prey. It is in guiding his initial steps along these lines that the librarian can best serve the historical collection.

[4] *Bulletin of the Johns Hopkins Hospital*, 1930, vol. 46, p. 61.

In making plans for the post-war world we hear so much about, it is clear how the librarian can chart the proper course. The physician, too, can look ahead. It is to be hoped that in peace time more medical schools will offer courses in the history of medicine, or if not, that courses on various medical subjects may be introduced by historical summaries. Then the professor can urge his student to visit the historical collection, perhaps even to write a brief paper on some specific phase of the subject. The more specific his topic, the more will he learn, the more fully can he treat it. In this way, and with the librarian's help, the student becomes familiar with the historical books and their use.

Some method should be devised for the rousing of the physician as well as the student. A most profitable and workable solution might be the organization of a board of consultants, a board composed not of two or three men, but of a larger group, on whom the librarian could rely for occasional assistance. A physician might be selected from each medical specialty, one who had some interest in its history. The librarian would then be able to turn to members of this group when emergencies arose, and the men would surely feel active partners in the development and operation of the library. This is as it should be. I am sure that many physicians would be glad to give of their time and knowledge but hesitate lest the librarian resent intrusion or criticism, while the librarian often feels presumptuous at the thought of interrupting a busy man's practice.

The medical library exists for the medical man and he should learn that the more he contributes to it, the better it will serve him. The historian, completely dependent upon the library for his tools should be even more aware of this. Mutual effort on the part of physician and librarian can achieve our ideals, but neither one nor the other can succeed alone, and this should be given due thought in our many plans for the not too distant future.

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